REMARKS/ARGUMENTS

Claims 1, 3-14, 17-65, and 67-70 are currently pending in the above-identified application. The Examiner has withdrawn claims 17-20, 23, 24, 28-41, 44, 45 and 70 as directed to a non-elected invention. Applicants mote that claims 28-35 should not be withdrawn in their entirety as they should be considered encompassed within the elected invention when limited to a composition and method using HIV-1 antigen of SEQ ID NO:2. See Group II as set forth on page 2 of Paper No.9. Therefore, Applicants respectfully request that claims 28-35 be considered as part of the present invention. By this amendment claims 17-24, 36-45, 47-49, 52, 53, 57, 65, 66 and 70 have been cancelled without prejudice to renewal of prosecution of the subject matter encompassed by any cancelled claim in a related copending application. Further, by this amendment claims 1, 25, 46, 50, 54, 58, and 63 have been amended. Support for these amendments is more fully set forth in the following remarks. No new matter has been added by these amendments. Claims 1, 3-14, 25-35, 46, 50, 51, 54-56, 58, 59-64 and 67-69 remain pending.

Applicants acknowledge the finality of the restriction requirement and that the Examiner has withdrawn claims 17-20, 23, 24, 28-41, 44, 45 and 70 from prosecution as drawn to a non-elected invention. The Examiner has also required cancellation of the non-elected claims in order to provide a complete reply to the present final rejection. As above, Applicants have cancelled claims 17-20, 23, 24, 36-41, 44, 45 and 70, but believe that claims 28-35 as drawn to a composition and method using HIV-1 antigen of SEQ ID NO:2 were not properly withdrawn. As claims 28-35 have been amended to recite "a chimeric peptide having the amino acid sequence KQIINMWQEVGKAMYAPPISGQIRRIQRGPGRAFVTIGK (SEQ ID NO: 2)"

these claims are properly within the elected invention. The Examiner is respectfully requested to reconsider withdrawing these claims.

Further, the Examiner has noted that a copy of the abstract for the application on a separate sheet was not attached to Applicants' prior response. Applicants attach to this response a copy of the abstract for the present application as filed with the US Receiving Office of the United States Patent Office on September 11, 1998 and published as WO 99/12563.

Applicants note the withdrawal of the rejection of claim 49 and 55 under 35 U.S.C. § 112, second paragraph. The withdrawal of the rejection of claims 46-65 and 67-69 under 35 U.S.C. § 103(a) as obvious over Ahlers *et al.* is also noted.

Rejections Under 35 U.S.C. § 101:

Claims 1-14, 21, 25-27, 42 and 43 remain rejected under 35 U.S.C. § 101 because the Examiner believes the claimed invention is not supported by either a credible asserted utility or a well established utility. In particular, the Examiner continues to assert that the invention is directed to methods and compositions that provide a clinically effective protective vaccine in humans and that the specification does not support the reducing, inhibiting, or killing of free HIV-1 or infected cells *in vivo*. In addition, the Examiner continues to assert that the specification does not provide evidence that the CTL response induced by the method of the instant invention reduce or kill HIV in the rectal mucosa or systemically and further, that "the elected peptide of the claimed method uses a specific sequence and, given the variation in HIV, there is no evidence that it is able to reduce, inhibit or kill HIV-1 of the immunogen stain, let alone different strains." The issue of immunosuppression, at least as it applies to the elected

sequence, has been withdrawn, but the Examiner has maintained that the induction of a CTL response can not be assumed to reduce, inhibit or kill HIV-1.

The Examiner has considered the journal article by Belyakov *et al.*, previously submitted by Applicants, as evidence of either a credible asserted utility or a well established utility, but has not found the evidence presented as persuasive. In particular, the Examiner does not believe the results necessarily correlate with the claimed invention because the peptides used are different from those claimed in the present invention. In support of the reasoning the Examiner has cited to page 609 of Lee, *in* "AIDS, Biology, Diagnostics, Treatment, and Prevention", fourth edition, DeVita *et al.* editors, Lippincott-Raven Publishers, 1997, pages 605-661, which purportedly teaches that "[h]owever, there is no convincing basis to conclude that protection observed in any of the animal models is suitable to predict vaccine efficacy in humans." The Examiner also has asserted that "Belyakov el al. teach a specific adjuvant that is not claimed and may well play a critical role in the resulting immune response."

Applicants have amended claims 1 and 25 to recite "[a] method for inducing an antigen specific systemic and rectal mucosal cytotoxic T lymphocyte (CTL) response in a mammalian subject comprising contacting a rectal mucosal tissue of the subject with a composition comprising a chimeric peptide having the amino acid sequence KQIINMWQEVGKAMYAPPISGQIRRIQRGPGRAFVTICK (SEQ ID NO:2)." This amendment makes the pending claims in the application consistent with the restriction requirement of the Examiner in this application that a method for contacting each and every peptide with the rectal mucosa to induce a CTL response constitutes a patentably distinct invention. Further, the claims have been amended to delete the phrase "wherein the contacting induces a systemic and rectal mucosal cytotoxic T lymphocyte response that can reduce

proliferation of a virus expressing the CTL activating epitope of the HIV isolate." This phrase has been deleted as redundant.

Applicants must again disagree with the Examiner that the generic invention previously claimed and the specific invention of the claims now pending in the application are not supported by either a credible asserted utility or a sell established utility. The assessment of whether an applicant has satisfied the utility requirement is focused on the claimed invention. Further, where an applicant has established utility for a species that falls within an identified genus of compounds, and presents a generic claim covering the genus, as a general matter, that claim should be treated as being sufficient under 35 U.S.C. § 101. Also, an applicant need only make one credible assertion of specific utility for the claimed invention to satisfy 35 U.S.C. § 101 and 35 U.S.C. § 112; additional statements of utility, even if not "credible," do not render the claimed invention lacking in utility. MPEP 2107.02(I).

The Examiner appears to have analyzed the claims to only have utility as a method or composition that provides a clinically effective protective immunity against HIV-1 or even that the claimed methods and compositions must "cure" AIDS. For example, the Examiner has again stressed that "Applicant has not demonstrated protection from HIV of any isolate" and that because HIV "can linger in immuno-privileged sites and can remain quiescent . . . the invention would not be effective at reducing, inhibiting, or killing HIV-1." Applicants believe that these results or limitations have been inappropriately read into the claims and used in the analysis of whether the claimed invention is supported by an asserted credible or well established utility.

The induction of a cytotoxic T lymphocyte response is well known can clear viral infections and that CTL can lyse infected target cells early in infection before they can produce

viral progeny that might be released by cell lysis. See Berzofsky and Berkower, *AIDS* 9(suppl A):S143-S157 (1995); Reference AN, Information Disclosure Statement filed August 17, 2000). Berzofsky and Berkower also disclose that "trials of adoptive transfer of *ex vivo* expanded autologous polyclonal HIV-specific CTL in HIV-infected patients are in progress, and preliminary results suggest some potential benefit (Lieberman *et al.*, *AIDS Res. Hum. Retroviruses* 10(suppl 3):S110." Further, Lee, cited by the Examiner, states at page 613, left column in the section entitled "Vaccine Efficacy" that "it appears that preventing disease progression should be considered a valid measurement of the efficacy of an HIV vaccine" and that "preparations that elicit broadly neutralizing antibodies or CTLs to HIV may also have the potential to delay progression to AIDS." Also, at page 51, line 8 through page 52, line 6 of the specification the reasoning why the induction of an antigen specific systemic and rectal mucosal cytotoxic T lymphocyte response in a subject is a credible utility and/or a well established utility. Applicants believe that any artisan skilled in the art would consider that the claimed methods and compositions of the present invention have a credible or well established utility.

Applicants believe that each of the reasons raised by the Examiner in support of the rejection under 35 U.S.C. § 101 are not directed to the invention as claimed and are not relevant to the analysis of support for the invention. In particular, a showing of protection from HIV of any isolate is not required, nor is, cell to cell transmission of HIV effect the ability of the present invention to induce the response claimed. Further, the existence of any latent HIV in an immuno-privileged space does not indicate that the claimed methods and compositions induce an antigen specific systemic and rectal mucosal cytotoxic T lymphocyte response is not supported by a credible or well established utility. The existence of latent HIV would appear to pose a possible question of whether any immunological method would "cure" AIDS. The induction of a long lasting antigen specific systemic and rectal mucosal CTL response, as demonstrated in the

specification would appear to be a means to prevent such latent virus from expanding from such an immuno-privileged space into the circulatory system and contributing to the progression of disease.

The Examiner has submitted a review article by Lee as evidence that testing with SHIV in monkeys is not the same as HIV in humans and that there is no convincing basis to conclude that protection observed in any of the animal models is suitable to predict vaccine efficacy in humans. As above, Applicants do not claim a method or compositions that induce a protective immune response to HIV-1 or any other organism. The Examiner has not provided any evidence that an animal model is inappropriate for demonstrating that a particular peptide or a homologous region of a peptide derived from HIV or SIV can not be extrapolated to humans. The peptide of the present invention comprises epitopes that bind to MHC class II (HLA) molecules of multiple haplotypes and to be recognized by $CD4^+$ helper T cell precursor cells and epitopes that are recognized by cytotoxic T lymphocytes of infected individuals. Homologous epitopes are known for the envelope protein of SIV. The Examiner has not provided any reasoning why a peptide comprising these epitopes from SIV, HIV or a chimeric with epitopes from SIV and HIV when used in an appropriate animal to induce an antigen specific systemic and rectal mucosal cytotoxic T lymphocyte response would not extrapolate to a similar result in humans. Therefore, the Belyakov *et al.* article is relevant to whether the pending claims are supported by an asserted credible utility or a well established utility. Further, the Examiner has not provided any reasoning why the use of an unclaimed specific adjuvant might be critical in the resulting immune response. Applicants note that although the particular adjuvant, LT(R192G), is not claimed the adjuvant is a species of the claimed mutant *E. coli* heat labile enterotoxin. See claim 4. Further, the use of a particular adjuvant would only appear to relate to a question of sufficient efficacy of a method or composition which is not a proper basis for assessing untility.

Applicants respectfully request the Examiner to reconsider and withdraw the rejection of claims 1-14, 21, 22, 25-27, 42 and 43 under 35 U.S.C. § 101 in view of the amendments and remarks above.

Rejections Under 35 U.S.C. § 112, First Paragraph:

Claims 1-14, 21, 22, 25-27, 42 and 43 remain rejected under 35 U.S.C. § 112, first paragraph. In particular, the Examiner has maintained this rejection because he does not believe that claimed invention is supported by either a credible asserted utility or a well established utility for the reasons stated above and that one skilled in the art would not know how to use the claimed invention.

Applicants direct the Examiner to the above amendments and remarks and believe that one of skill in the art would know how to use the claimed invention. The skilled artisan has been provided with sufficient guidance how to use the claimed methods and compositions of the present invention to contact the rectal mucosa to obtained the claimed result. The Examiner is respectfully requested to reconsider and withdraw the rejection of claims 1-14, 21, 22, 25-27, 42 and 43 for the reasons set forth above.

Rejection Under 35 U.S.C § 102:

Claims 46-48 and 59 remain rejected under 35 U.S.C. § 12(b) as being anticipated by Ahlers *et al.* because the Examiner believes that the claimed invention is a composition comprising the same peptide as the prior art and that the prior composition is in a form suitable for rectal administration.

Although Applicants do not acquiesce to the rejection of the Examiner, but in order to further expedite prosecution of particular embodiments of the present invention, claim 46 has been amended to recite "[a]n immunogenic composition comprising a chimeric peptide having the amino acid sequence KQIINMWQEVGKAMYAPPISGQIRRIQRGPGRAFVTIGK (SEQ ID NO: 2), formulated for intrarectal delivery to the rectum, colon, sigmoid colon, or distal colon; wherein said composition is formulated as a rectal emulsion, foam, suppository, or gel preparation and comprises a base, carrier, or absorption-promoting agent adapted for intrarectal delivery." Support for this amendment can be found in claims 47, 48, 49, 52 and 53 which have been cancelled. Further, claims 50, 54 and 56 have been amended to change the dependency from a cancelled claim to currently amended claim 46. Also, claim 57 has been cancelled as redundant and claim 65 has been cancelled as directed to a non-elected invention. In addition claim 63 has been amended for clarity by deleting the phrase "to eliminate toxicity and enhance mucosal tissue bonding mediated by protein A" which is an unnecessary functional characteristic of the recited composition.

Applicants believe that amendment of claim 46 to recite the characteristics of claims 49, 52 and 53 renders the claims unanticipated by Ahlers *et al.* These particular types of compositions adapted for rectal administration are not suggested or disclosed by the reference and therefore, Applicants respectfully request the Examiner reconsider and withdraw the rejection of claims 46 and 59 in view of the amendments and remarks above.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an

early date is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,

Dated: 20 Oct 2003 By: _____
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